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THE "SCHICK" INOCULATION
FOR IMMUNISATION
AGAINST DIPHTHERIA

by

M. BEDDOW BAYLY, M.R.C.S., L.R.C.P.

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THE "SCHICK" INOCULATION FOR IMMUNISATION AGAINST DIPHTHERIA

An Exposure of its Dangers and Fallacies

by

M. BEDDOW BAYLY, M.R.C.S., L.R.C.P.

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SPECIAL NOTE REGARDING THE USE OF THE TERM "SCHICK."

The qualifying adjective "Schick" is, strictly speaking, only applicable to the skin test which was devised by Professor **Bela Schick** of Vienna in 1913, and has consequently borne his name.

But the term has become, by popular usage, so closely associated with the complete process of testing and immunising that for the purposes of this pamphlet it seemed to be of advantage to use it throughout for the immunising inoculation as well as for the preliminary test.

The reader will understand that wherever the term "Schick" occurs in inverted commas it is being used for convenience and not in a strictly scientific sense.

SECTION I.

THE GERM THEORY
OF
DIPHTHERIA

THE GERM THEORY OF DIPHTHERIA.

The attempt in recent years to prevent diphtheria by the injection of toxin-antitoxin and similar products, as well as the routine treatment of diphtheria, when it occurs, by antitoxic serum, is based upon the primary fallacy that diphtheria is caused by a "germ"—the Klebs-Loeffler bacillus.

The following facts prove that this belief is a fallacy :—

1. The germ is absent in many cases of the disease it is alleged to cause :

In 14 per cent. of cases, according to the *Lancet*, Sept. 1898, (p. 779)

In 20 per cent. of cases, according to the *Report of Royal Commission on Vivisection*, 1912 (p.38)

In 28-40 per cent. of cases, according to Sir William Osler, ("*Principles and Practice of Medicine*," 8th ed., 1912, pp. 58-60.)

2. It is commonly present in many diseases it is not supposed to cause. A list of 17 of these, ranging from Eczema to Endocarditis and from Pleurisy to Puerperal fever, will be found in the *Medical World* (June 15th, 1928, p. 330).

3. It is frequently found in the throats of normal healthy people. According to the *Ministry of Health Report* (No. 10, p. 26). it has been demonstrated in 15 to 20 per cent. of school children.

The same *Report* (p. 14) states that in the Willard Parker Hospital in New York, of 1,200 patients, 20 per cent. had diphtheria bacilli in their throats and were in contact with diphtheria cases, and yet in no single instance developed diphtheria, although in many cases the bacilli were of a virulent type.

Even "persons giving a positive reaction (Schick)", and therefore supposedly susceptible to attack, "may occasionally harbour diphtheria bacilli in their throats without developing diphtheria." No explanation of this has been offered. (*Report on Diphtheria*, by the Ministry of Health, No. 10, p. 13.)

In fact, as Dr. Claude Buchanan Ker, Medical Superintendent of the City Hospital, Edinburgh, wrote in his text-book, "*A Manual of Fevers*" (1912) :—

"It is certain that a healthy mucous membrane is capable of resisting diphtheria and many persons in perfect health harbour the bacillus in the throat." (p. 224.)

4. The germs are innocuous when experimentally introduced into the healthy body.

(a) Dr. Rodermund "sprayed the poisons of diphtheria, smallpox, scarlet fever, or consumption into the throat, nose [of

his patients], or had them breathe into the lungs, repeating the experiments in most cases every one or two weeks for months with the result that no disease could be developed." (*Medical Brief*, St. Louis, U.S.A., 1906.)

(b) Dr. Fraser, of Toronto, and five volunteers swallowed millions of active Klebs-Loeffler bacilli in milk, bread, fish, and alone, without any subsequent ill-effects. (*Canadian Lancet*, 1917.)

(c) Professor Ulrich Friedemann, M.D., Berlin, has stated :—

" It is known that diphtheria bacilli do not live long in a healthy organism." (*The Lancet*, Aug. 4th, 1928, p. 214).

5. It is clear that the claim of the Klebs-Loeffler bacillus to be considered the causal agent in the production of diphtheria is unsupported by scientific evidence. As Professor Friedemann affirmed when dealing with its almost ubiquitous nature :—

" We came to the conclusion that in one year about one-third of the population is infected with diphtheria bacilli without contracting the disease." (*Loc. cit.*)

The part played by the bacillus in the transmission of the disease from one person to another is equally in doubt. Professor Friedemann reported that after investigation Doull and Lara

" Came to the conclusion that the danger of infection by carriers is negligible compared with the danger of infection by patients." (*ibid.*, p. 215).

Furthermore, in regard to the latter he admitted that as the result of a League of Nations inquiry among seven different nations :—

" We see that the number of case-to-case infections does not amount to more than 2.9 per cent. of the total diphtheria cases." (*Loc. cit.*).

6. No animal develops the signs and symptoms of diphtheria when experimentally injected with the germs. (*Report of Royal Commission on Vivisection*, 1912, p. 120.)

7. " Other microbes, such as the streptococcus, the tetragenus and the pneumococcus, take upon themselves occasionally to construct membranous formations on the tonsils . . . not to be differentiated clinically from diphtheria . . . they may be accompanied by glandular masses and suppuration." (*The Franco-British Medical Review*, Dec. 1924, Vol. I., No. 3, p.47.)

The Klebs-Loeffler bacillus, therefore, clearly fails to fulfil a single one of the conditions which would establish it as a causal agent in diphtheria, and were laid down as the essential requirements of the Germ Theory of disease by Koch and Pasteur, the originators of that theory.

SECTION 2.

THE SERUM TREATMENT
OF
DIPHTHERIA

2. The favourable statistics were brought about largely by the change of diagnosis from the clinical to the bacteriological.

"As a result of this change of view, cases of mild sore throat are now classed as diphtheria—cases which would, in any case recover, whatever the treatment; and the fatality of diphtheria will be reduced accordingly." (Editorial in *The Lancet*, Nov. 4th, 1904, p. 1342.)

Recent confirmation of this is afforded by Prof. W. W. C. Topley, who, in his recent work, "*An Outline of Immunity*," refers to this change in the basis of diagnosis, and states:—

"For this reason, the total of recorded cases would tend to be increased by the inclusion of many mild infections, and the recorded case-mortality would automatically fall."

As a result, statistics of the case-fatality rates of diphtheria throughout the world have been invalidated.

3. On the other hand, the total deaths from diphtheria per million of the population increased after antitoxin was introduced:

In the 30 years prior to 1894 (when serum was introduced) deaths from diphtheria in England and Wales were 4,676.

In the 30 years subsequent to 1894, the deaths were 5,197.

In the case of measles, whooping cough and scarlet fever the analogous figures of mortality show, in comparison, a very large reduction; and this took place without the use of any serum in these diseases.

4. Finally, the claim that antitoxin has any beneficial effect at all on the fatality is completely disproved by a comparison of the percentage of deaths among the inoculated with that of the uninoculated; the figures are given in the *Report* of the Metropolitan Asylums Board for 1910, and show that during the previous ten years

Among 50,000 cases treated *with* serum the deaths were 11 per cent.

whereas

Among 6,800 cases *without* antitoxin the deaths were 3 per cent.

The figures are all the more remarkable when it is realised that, according to this Report itself, cases too advanced to be given serum are included in the non-inoculated class.

RECOGNITION OF THE FAILURE OF SERUM WORLD-WIDE.

So signal a failure has antitoxin proved to be in diphtheria that on all sides disappointment is being expressed by medical authorities.

1. Thus the *Annual Report of the Metropolitan Asylums Board* (1924-25), states:—

"There is a popular tendency to class diphtheria with . . . other infectious diseases as one that medical science has definitely controlled and robbed of most of its terrors. That, however, is far from being the case, . . . the fact remains that for reasons not altogether clear, diphtheria appears to be strengthening its forces and gathering power, *unchecked by Science.*" (p. 30.)

2. Dr. Cameron Kidd, M.O.H. for Bromsgrove, declared himself "disillusioned" in the *Brit. Med. Jour.* of August 29th, 1925:

"No one," he said, "will, I think, deny that the promise of twenty years ago, when antitoxin treatment was first adopted, that diphtheria mortality would be greatly diminished, has not been fulfilled." (p. 398.)

3. *The Lancet*, July 7th, 1928, in a leading article, referred to the early days of antitoxin when "there seemed no doubt that diphtheria was conquered," and confessed:—

"With the passing years these hopes have not been realised, . . . The incidence of diphtheria not only remains high, but in London, has for many years been steadily rising, whilst the case-mortality has shown an alarming increase in Germany and other countries where serum treatment has long been employed as a routine." (p. 21.)

4. The M.O.H. for West Lancashire Rural District reported in the *Manchester Guardian* of June 16th, 1930, that

"never in the history of the Council's Isolation Hospital had it been necessary to perform so many tracheotomies."

5. *The Lancet* of March 14th, 1931, reported "the extraordinarily severe epidemic of diphtheria which has recently occurred in Berlin and the high case-mortality in spite of the large doses of antitoxin given at an early stage of the disease." (p. 598.)

6. Dr. Friedemann, of Berlin, was quoted in *The Lancet* of August 4th, 1928, as saying that the case-mortality of diphtheria used to be 4-7 per cent.; since 1926 it had risen to 25-35 per cent. "Even patients injected with large doses of serum on the first day," he declared, "have succumbed within 24 hours." (p. 212.)

The incidence of diphtheria in the German Reich during 1931, 1932 and 1933 are given by the Berlin Correspondent of the *Jour. of the Amer. Med. Assoc.*, May 12th, 1934 (Vol. 102, No. 19, p. 1626), as follows:—

			1931	1932	1933
Cases	56,627	64,138	74,559
Deaths	3,095	2,974	3,628

7. The *Medical World* of April 29th, 1932, announced that "diphtheria, save for the brilliant exception of America, is everywhere increasing in frequency and deadliness." (p. 159.)

8. The alleged brilliance of American success with serum is dimmed by the report in the *New England Journal of Medicine*, of February 1st, 1934 (p.275). We are told in the editorial that :—

"There are, however, as the Bulletin of the Metropolitan Life Insurance Company points out, a number of States and large cities where the diphtheria death-rate is to-day not only disgracefully high, but actually increasing."

"The 1932 figure was actually 34 per cent. higher (in four States) than prevailed for the registration area of the United States for *ten years previously*."

9. Dr. Louis Cobbett, in the *Brit. Med. Jour.* (July 22nd, 1933) deplored the fact that antitoxin, so wonderfully effective in the laboratory, has had such a comparatively small effect in lowering the death-rate from diphtheria during the last 40 years. (p. 140.)

CLAIMS VERSUS FACTS

The foregoing authoritative evidence regarding the failure of antitoxin is a complete refutation of the claim made by Sir Arthur Newsholme, K.C.B., M.D., F.R.C.P., in his book, "*The Story of Preventive Medicine*." (1929).

"The discovery of antitoxin for diphtheria was a triumph of laboratory research, the outcome of experimental work on immunity; the progress of this research can be seen from stage to stage, and it constitutes an epochal point in the history of medicine."

No more damning commentary on the fallacies and failures of such medical research (vivisection) could be imagined than that afforded by the evidence contained in this pamphlet, which has been derived entirely from sources of unimpeachable authority.

SECTION 3.

THE HARMFUL EFFECTS OF SERUM
IN THE
TREATMENT OF DIPHTHERIA

THE HARMFUL EFFECTS OF SERUM TREATMENT

The following dangers are inherent in the practice of serum-therapy itself, and are not in any sense due to errors in manufacture, or storage, or of administration to the patient by the doctor.

They fall under three main headings:—

1. *Immediate.* This may take the form of sudden collapse and may sometimes be followed rapidly by death.
2. *Delayed.* This may take the form of: (a) rashes, joint pains, etc., which may occur after a few days; (b) a state of hypersensitiveness known as "anaphylaxis", which may lead to severe illness, prostration and death.
3. *Remote.* This may take the form of numerous chronic and intractable types of disease which, as often as not, are never traced to their true source.

Let us examine these in greater detail.

1. Many cases of sudden collapse and death in previously healthy individuals, following injection with serum as "contacts," have been recorded in the medical press ever since the classical instance of the death of Dr. Robert Langerhans' own son a few minutes after a prophylactic dose of anti-diphtheritic serum in 1896. (*Serums, Vaccines and Toxins*, W. Cecil Bosanquet and J. W. H. Eyre, 1916, p.126.)

In 1924 Lamson collected data of forty-one similar deaths due to the administration of sera. (*Journal of the American Medical Association*, April 5th, 1924, p. 1091.)

Numerous instances occurred during the Great War, both in horses and troops, but in the general carnage little interest was aroused.

In the *Medical Press and Circular* of January 19th, 1927, the statement is made that "It is almost always with anti-tetanic or anti-diphtheritic serum that fatal accidents or paralysis are observed." (p. 51.)

The most recent case reported was that of a fourteen-year-old boy, an inmate of the Bramhope Branch of the National Children's Home. It was reported at the inquest that he died within a few minutes of being given an injection of serum as a prophylactic against scarlet fever. (See *The Lancet*, 20th October, 1934, p. 897.)

SERUM DISEASE

2. (a) Serum Disease, which occurs in about 40 per cent. of the inoculated, has been investigated by many workers since it was first studied by von Pirquet and Schick in 1903-4. The widespread use of anti-toxic sera in diphtheria has resulted in a large increase in the actual incidence of this condition according to Dr. Mitchell, who declared a few years ago that it was "evident that some factor is operating to cause an increase in the incidence of

serum-disease, and that *refinement of serum alone will not solve the problem*" (my italics). (*Journal of the Medical Society of New Jersey*, January, 1930.)

In the *Medical Press and Circular*, January 19th, 1927 (p.51), it is estimated that serum reactions occur in 12 to 15 per cent. of cases of children after the first injection, rising to 50 per cent. of subsequent ones, and in 75 per cent. of adults.

Even higher figures are mentioned in the *Epitome of the British Medical Journal*, December 31st, 1932 (p. 109). Statistics from a Chicago hospital, collected over a period of 19 years, show that reactions occur in 28.1 per cent. of cases with diphtheria antitoxin, 22.7 per cent. with scarlet fever antitoxin, and 81 per cent. with meningococcic serum.

The symptoms usually arise some three to fourteen days after the injection of the serum. They formed the subject of an interesting monograph in 1918 by Dr. E. W. Goodall, who collected and published observations on 3,500 cases of serum sickness following injections of diphtheria antitoxin. (*The Lancet*, March 2nd, 1918, p. 323.)* They consist of rashes, generally urticarial in character, severe joint pains, glandular enlargement, abscesses at the site of the injection (even when strict asepsis has been observed), pyrexia, cardiac paralysis, vomiting and diarrhoea.

According to Dr. J. H. Whitaker, Medical Superintendent of the Grove Fever Hospital, London,

"The symptoms met with in serum sickness are now much more severe than in former times, especially in the case of adults. In addition to the usual well-recognised symptoms of serum sickness, it is now not at all uncommon to meet with vomiting and acute abdominal pain—two very unsatisfactory symptoms in diphtheria—and in a few cases I have lately met with hæmaturia, jaundice, extensive subcutaneous hæmorrhages, and suppurative cervical adenitis. (*Practitioner*, Oct. 1926, p. 229.)

Dr. L. J. Witts, Assistant Physician at Guy's Hospital, in the course of a clinical lecture delivered in January 1931, on "Fallacies and Dangers in Treatment," referred to this danger in the strongest terms. Though an advocate of serum-therapy, he warned against the indiscriminate use of serum, for, he said:—

"You expose your patient to the risk of an immediate serum accident; you may inflict on him the painful disease of serum-sickness, in which the tortures of the cutaneous irritation, and the swollen joints may be almost unbearable, and finally you sensitise him to serum so that his life may be imperilled in the hour of need, when it may be essential to inject a potent serum." (*Medical World*, Jan. 23rd, 1931, p. 566.)

*See also Article by Prof. Bezançon, Physician to the Hospital Saint Antoine, Paris, in *Franco-British Review*, Sept., 1928, p. 263; also article on "The Nature and Clinical Significance of Anaphylaxis," by J. Chamberlain, M.R.C.S., L.D.S., in *The Medical World*, January 2nd, 1931 (p. 469).

The last sentence of Dr. Witts' warning brings us to the next danger.

(b) The first dose of serum, though causing no reactions of a severe nature itself, produces a condition in the patient of hyper-sensitiveness to any serum derived from the same animal; this condition is known as "anaphylaxis," and may result, when a second injection of serum takes place, in collapse or death of the patient, just as in the case of serum injected for the first time. (See under 1.)

Instead of collapse or immediate death, however, a condition may be locally set up at the site of the injection, which is known as the *Arthus Phenomenon*, and consists in *mass gangrene* of more or less extensive areas; this process will be found more fully described, with illustrations of actual cases which occurred as the result of the injection of TOXIN-ANTITOXIN, in the section which deals with the dangers of IMMUNISATION mixtures. (See p. 44.)

It is significant to find J. Chamberlain, M.R.C.S., L.D.S., declaring before Guy's Hospital Physical Society in 1931, that :—

"The increasing frequency with which human interference permits injections of antigenic substances into the circulating blood, betokens an increasing number of fatal anaphylactic reactions and other less significant forms of sensitisation." (*Medical World*, Jan. 2nd, 1931, p. 476.)

REMOTE EFFECTS OF SERUM

3. The more remote effects of serum inoculation have been emphasised by J. E. R. McDonagh in his most recent writings. His unique work on the chemico-physical properties of the blood, especially in regard to the colloidal protein particles, is worthy of the closest study. One of his particularly pertinent statements is as follows :—

"Serums are very liable to give rise to shock, and to the more obvious manifestations produced the term 'anaphylaxis' is usually applied. Owing to the peculiar constitution of the protein the appearance of *the signs and symptoms of shock may be delayed months and even years*, and the longer the delay the more difficult grows the problem of combating them. The long delay frequently *results in the manifestations of chronic disease, which, as often as not, remain for ever unconnected with the cause*. When death occurs, it does so slowly, and after a long period of time. . . ." (My italics.) (*Nature of Disease Journal*, Vol. 2, 1933, p. 126.)

SECTION 4.

THE SCHICK TEST.

THE SCHICK TEST

The Schick test consists in injecting a small quantity of the toxin of the Klebs-Loeffler bacillus into the skin, and is therefore based on the fallacy that the germ is the cause of the disease.

According to a *Memorandum* drawn up by Dr. Ker, Medical Superintendent of the Edinburgh City Fever Hospital,

"By the use of a simple test, it is possible to find out those children who are liable to take the disease and those who are not." (*The Lancet*, Nov. 8th, 1924, p. 950.)

A positive reaction, it is claimed, indicates susceptibility; a negative reaction, immunity from diphtheria.

1. THE TEST IS OF NO VALUE IN CHILDREN UNDER FIVE (when it is most needed).

Dr. J. A. Nixon, Physician to the Bristol Infirmary, stated that

"The (Schick) test was of no value in children under five years of age . . . and it gave no evidence as to the virulence or avirulence of any infection." (*Brit. Med. Jour.*, July 7th, 1923, p. 20).

2. THE TEST IS BEING ABANDONED IN NEW YORK AND OTHER PARTS OF AMERICA, ON ACCOUNT OF ITS UNRELIABILITY.

We find Dr. Louis van Boeckel reporting to the League of Nations Health Organisation in 1924 that

"The tendency at present (in America) is to omit the preliminary Schick test."

The following year, 1925, the *Annual Report of New York City* declared that the test had been abandoned (p. 114).

In the (American) *Medical Journal and Record*, March 3rd, 1926, it is stated :—

"There is a growing feeling among Public Health workers that the Schick test should be abandoned in the immunization of large groups of children. In fact, there are those who believe it is a useless procedure both in private and public health practice." (p. 332.)

3. THE RESULTS OF THE TEST VARY ACCORDING TO THE FIRM SUPPLYING THE MATERIAL.

Dr. Peters, of Bristol University, found that test material from two different firms, when tried on the arms of 11 individuals gave in one case 8 positive reactions and 3 negatives; in the other, 5 positives and 6 negatives. "An alarming disparity," he remarked. (*The Lancet*, October 6th, 1923, p. 784.)

4. SCHICK NEGATIVE PEOPLE CONTRACT DIPHTHERIA.

Dr. Forbes in his book on diphtheria ("Diphtheria, Its Distribution and Prevention," 1932) admits that :

"The immutability of the negative reaction is not always to be depended on as a *constant* index of immunity." (p. 809.)

He goes on to say that

"Results, which have been accumulating during recent years, have shown, notably in the cases of Schick-testing of members of Hospital nursing staffs, that occasionally primary Schick-negatives, and those who have been immunised and have subsequently yielded a negative reaction, may contract diphtheria." (pp. 809-10.)

In Dr. Forbes's records there are 115 cases of diphtheria in primarily Schick-negative persons, and 31 cases in persons found to be Schick-negative after a course of three or more injections.

Dr. William Robertson, in his *Annual Report for Edinburgh* (1927) reported 58 cases of diphtheria among Schick-negative children.

The *British Medical Journal*, July 17th, 1926 (*Epitome of Current Med. Lit.*, p. 9), quotes from a Munich medical journal a doctor who "has recently observed 12 cases of diphtheria in children with a negative Schick reaction."

Dr. Massingham, R.M.O. of the London Fever Hospital, reporting on four nurses who, although tested and found Schick-negative (two immunised), developed diphtheria, concludes that :

"There are people who, although susceptible to diphtheria, may yet give a negative Schick reaction." (*The Lancet*, Feb. 25th, 1928, p. 416.)

5. SCHICK POSITIVE PEOPLE DO NOT CONTRACT DIPHTHERIA.

(a) According to the *Ministry of Health Report on Diphtheria*, No. 10 :—

"... persons giving a positive reaction may occasionally harbour diphtheria bacilli in their throats without developing clinical diphtheria." (p. 13.)

No explanation of this anomaly has been offered.

(b) Dr. Massingham, Resident Medical Officer of the London Fever Hospital, writing in *The Lancet*, February 25th, 1928, admitted that

"All Schick-positive people, although constantly exposed to massive doses of infection, do not contract diphtheria ; and that a positive reaction with virulent diphtheria bacilli in the throat is compatible with perfect health." (p. 416.)

6. RESULTS OF TEST IN LARGE NUMBERS OF SCHOOL CHILDREN IN CONFLICT WITH EXPERIENCE.

It is claimed that as a result of tests in this country and America, the children of better-class households are more sus-

ceptible to infection than those of the poorer classes, since the latter gradually become immunised through constant contact with infection.

Tests carried out on large numbers of school children in 16 different types of school by W. T. Benson, M.D., D.P.H., Assist. M.O.H. for Edinburgh, and reported in *The Lancet*, November 8th, 1924 (p. 952), showed that children attending the schools serving the better-class neighbourhood were over two-and-a-half times as susceptible to diphtheria as those coming from a slum area.

The logical conclusion to be drawn from this would be to encourage the slums and pull down the better-class houses, in order to increase resistance to infectious disease. The manifest absurdity of this whole theory is borne out by vital statistics, *e.g.*

(a) G. Chesney, M.B., B.Ch., D.P.H., gives the following result of Schick tests (*Medical World*, May 13th, 1932, p. 206):—

Poole elementary school children : 18.7% negative (insusceptible)

London elementary school children : 54.27% negative.

Yet we find the less susceptible schools have higher attack-rates :—

Diphtheria attack-rate (average) per 1,000 in Poole	
in 1911-20	1.48
in 1921-28	0.57
Diphtheria attack-rate per 1,000 in London in 1911-20	3.05
1921-28	2.86

(b) The Registrar-General in his *Statistical Survey* for 1930 gives the following comparative figures for incidence of diphtheria :—

Cases under 15 per 10,000 population in London	...	132
in County Boroughs	...	83
in other urban districts	...	70
in rural districts	...	50

He comments :—

“ It will be seen that the excess of prevalence in London falls into line with large excess for great towns over small, and for small towns over rural areas, in all parts of England.” (p. 42.)

This disproves the theory that crowded conditions provide a natural immunity through “ contacts.”

(c) Austin Priestman, M.B., D.P.H., M.O.H. for Folkestone, writing in the *Medical World*, February 6th, 1931, on the incidence of diphtheria in schools, states that it was observed to be highest “ in those schools where sanitation is most deficient and ventilation and lighting the least satisfactory. The brightest and airiest school showed the least incidence, and the incidence throughout all the schools placed them in exact order of sanitary virtue. Moreover, the incidence indicated the schools where malnutrition in the children is most conspicuous.” (p. 627.)

7. SCHICK NEGATIVE PERSONS MAY BECOME POSITIVE.

(a) Austin Priestman, M.B., D.P.H. (in the *Medical World*, February 6th, 1931), writes :—

" This would seem to point to the conclusion that a Schick-negative can become Schick-positive, and is now doing so with greater frequency than we have hitherto imagined possible." (p. 627.)

(b) Drs. Young and Cummings in the *Journal of the American Medical Association* (February 18th, 1933, p. 530), maintain that

" Both artificially produced negatives and natural negatives tend to become positive over a given period of time."

(c) Dr. Matthew Burn, Chief Assistant Medical Officer of Health for Birmingham and Dr. Vera Fellowes, Assistant Medical Officer for Immunisation and Maternity and Child Welfare, described in the *Medical Officer*, July 11th, 1931, their experiences in the re-testing of Schick negative children in schools. They wrote :—

" Do we not see that some 50 per cent. of children who on a given date are primary negative reactors, and therefore, hitherto considered immune, may when tested at a later date, show positive reactions? Can any great reliance be placed, therefore, on the interpretation of the reading of the test, as indicating permanent immunity. . . . ? "

(d) In the Editorial of the *British Medical Journal*, June 16th, 1934, p. 1082) we may read :—

" Ten per cent. of boys artificially made Schick-negative may become Schick-positive in from six months to four years . . . "

8. TEST OF NO VALUE BUT STILL ADVOCATED.

Dr. J. R. R. McDonagh in the *Nature of Disease Journal*, (vol. I, p. 143) declares :—

" The most commonly performed immunity reaction is the skin test, which depends upon the production of a wheal . . . the test is of no value."

Yet, in spite of all this, Messrs. Burroughs, Wellcome & Co., in their recently-issued directions (6689H/J.786) for using their diphtheria prophylactic, make the statement that :

" It is never safe to assume immunity after immunization unless proved by a subsequent Schick Test."

Recently, too, Dr. W. A. Murphy, M.O.H., writing in the *Medical Officer* (July 21st, 1934), stated :—

" Diphtheria immunization without re-testing is not a scientific procedure and should not be practised."

SECTION 5.

“ SCHICK ” IMMUNISATION

IMMUNISATION

This consists of a series of injections into the skin, at variable intervals, of the TOXIN derived from the Klebs-Loeffler bacillus prepared in various ways, either alone or mixed with a certain quantity of antitoxic serum (from a horse).

(a) Between 1913 and 1924, according to Dr. Abraham Zingher in the *New York State Journal of Medicine* (February, 1934), some 14 varieties of toxin-antitoxin had been in use in New York.

(b) Toxoid is toxin treated by heat and formalin to render it less dangerous. It is known as Anatoxin (Ramon) on the Continent.

(c) Because of the possibility of Toxoid reverting to Toxin, it has frequently been mixed with antitoxin, and the resulting toxoid-antitoxin mixture is the one most commonly in use in this country, according to Sir George Newman's Report in 1926, and Sir Hilton Young in the House of Commons, March 15th, 1934.

(d) Alum-toxoid, toxoid-antitoxin floccules, and toxoid alum-precipitated are three further variants devised with a view to avoiding some of the more distressing reactions of their predecessors.

Nevertheless, the latest Memorandum issued by the Ministry of Health (170/Med. November, 1932) gives no guidance as to the use of any particular preparation, but leaves public health authorities to order any of the substances in question through the manufacturing chemists and importers, of whom it supplies a list.

Each of the foregoing substances has been in turn declared by the manufacturers harmless and effective, but in spite of laboratory tests and assertions, a long series of tragedies has occurred in various parts of the world since 1919. (See p. 32 post.)

THE FAILURE OF IMMUNISATION

The normal variation in the incidence of diphtheria is so great from year to year and from place to place that only statistics dealing with large numbers can be considered reliable evidence.

1. The *Deutsche Medicinische Wochenschrift*, November 25th, 1932, reports that of 100,000 children who had been immunised with three injections 10 per cent. contracted diphtheria. (See *Brit. Med. Jour.*, March 11th, 1933: *Epit. of Curr. Med. Lit.*, p. 39.)

Note: this would be a high percentage among non-immunised children.

2. In the *Bulletin of Hygiene*, March 1933, the following comment appears in the section dealing with "Infective Diseases":—

"It is pointed out that in Rome, where 28,340 children were immunized in the three years 1929-31, both the morbidity and mortality-rates from diphtheria have slightly increased rather than decreased during the period."

3. Dr. J. Graham Forbes, in his monograph, "*The Prevention of Diphtheria*," published by the Medical Research Council in 1927, tells us:—

"An extensive effort was set on foot in January, 1926, to eradicate diphtheria from New York State in the next five years."

Following successive years of decline both the cases and deaths increased in number, as the following figures (from *The Lancet*, May 18th, 1929, p. 1043), clearly show:—

Year	Cases	Deaths
1926	7,530	477
1927	13,500	717
1928	10,776	642

The writer of the "*Weekly Bulletin*," New York City Dept. of Health, had already commented in June, 1927:—

"I am at a loss to understand the increased mortality from this cause in view of the efforts made to toxin-antitoxinate many of the children in the city."

These efforts were fairly universal throughout the States, and the following figures, taken from the United States Public Health Service in "*Public Health Reports*" (February 10th, 1928), indicate the results:—

The total cases of Diphtheria in 37 States, with a population of 90,000,000		
in 1926	...	68,668
in 1927	...	80,152

A Report on the mortality rates in 93 cities of the United States, which is to be found in the *Journal of the American Medical Association*, May 26th, 1934 (p. 1758), gives tables showing the death rates in 5-yearly periods from 1890 to 1933. These indicate that the general decline which had occurred up to 1925 was in some cases maintained, but in not a few replaced by a considerable rise, especially in 1930.

There is, at all events, no evidence here that the advent of the practice of immunisation had any consistent effect on the death rates. Even in the *Report* itself the doubt is expressed whether the diminution may not be due "to the effect of a natural fluctuation in the prevalence or fatality of diphtheria." (p. 1758.)

Dr. E. Ashworth Underwood, in quoting statistics from New York, Chicago, Toronto and Hamilton, which had been published with a view to showing that immunisation had reduced the incidence of diphtheria in those towns, remarked:—

"Certain criticisms can be made of these results, and I am not yet certain they can be attributed solely, or even mostly, to mass immunization." (*Medical Officer*, May 26th, 1934.)

The New England Journal of Medicine (Vol: 210, No. 5, February 1st, 1934, p. 275), contains an editorial headed "The

Disgrace of Diphtheria," in which it is declared that "as the *Bulletin of the Metropolitan Life Insurance Co.* points out, there are a number of States and large cities where the diphtheria death-rate to-day is not only disgracefully high, but actually increasing."

"Four States in 1932 registered death-rates from diphtheria in excess of 13 per 100,000. In New Mexico, which with 19.5 per 100,000 had the highest rate in the country, the 1932 figure was actually 34 per cent. higher than prevailed for the registration area of the United States ten years previously."

"Thirty-two large cities had in 1932 diphtheria mortality rates above the average of 4.5 per 100,000, Knoxville leading the list with 17.0, Dallas [where the disaster occurred in 1919; see p. 32] being a close second with 16.6."

"The worst regional picture is that of the four East South Central States: Kentucky, Tennessee, Alabama [which reports severe reactions from alum-toxoid; see p. 41] and Mississippi, and the diphtheria situation in Oklahoma, Arkansas and Louisiana . . . is characterised as deplorable."

IMMUNISED PERSONS CONTRACT DIPHTHERIA.

1. In Dr. J. Graham Forbes' recent book on "*Diphtheria; its Distribution and Prevention*" there are reports of at least 330 cases of diphtheria that developed two months or more after the final inoculation.

2. The *Brit. Med. Jour.* of March 11th, 1933 (*Epit. of Cur. Med. Lit.*, p. 39), quotes the *Deut. Med. Woch.* (November 25th, 1932) as reporting 10,000 cases of diphtheria among 100,000 immunised.

3. According to the M.O.H. for Winnipeg, Dr. A. J. Douglas, of 268 cases of diphtheria (occurring between January 1st and November 30th, 1930) 17 had been immunised: 3 in 1925; 4 in 1926; 3 in 1927; 3 in 1928; and 4 in 1929. (*Report*, December 15th, 1930.)

4. The M.O.H. for Bristol, Dr. Davies, in *The Lancet*, November 21st, 1931, reported 44 children who developed diphtheria after having been fully immunised with three injections. Five of them had been "proved" to be immune by the Schick test. Nine were virulent, and one of them died 85 days after the third injection. He confesses:—

"It is disconcerting to find cases of clinical diphtheria occurring in Schick negative children and at such periods after the course. The periods varied from 185 to 204 days." (p. 1153.)

5. The M.O.H. for Cork, reporting on a "campaign of active immunisation . . . in which toxoid antitoxin was the prophylactic used," remarks that:—

"The success of the effort was greatly hampered by the continual occurrence of reported cases of diphtheria among treated or partially-treated children. It was in an attempt to prevent such cases that alum toxoid was introduced." (*The Lancet*, April 15th, 1933, p. 795.)

6. In the *Brit. Med. Jour. (Epit. of Cur. Med. Lit., p. 92)* of December 2nd, 1933, we may read :—

“ M. Fayot (Thèse de Paris, 1933, No. 487), who records 130 cases in patients aged from 14 months to 14 years in which diphtheria had occurred in spite of injections of anatoxin (toxoid), states that diphtheria in the inoculated occurs in about 3.3 per cent. of all the cases of diphtheria and has been noted in 11.6 per cent. of the cases at the Hôpital des Enfants Malades in Paris in recent years.”

7. According to the Winnipeg Department of Health and School Board Health Department, toxoid was introduced in 1925. In the succeeding 6 years :

Among 195,689 NON-immunised children there were 875 cases of diphtheria; that is, 447 per 100,000.

Among 11,259 Immunised children there were 52 cases of diphtheria; that is, 461 per 100,000.

8. A letter signed “ Medico ” in the “ *New York Medical Week,*” March 28th, 1931, reads :—

“ It might be interesting to note that the majority of cases of diphtheria which I have seen during the past year has been in children who have received toxin-antitoxin at the hands of our public agencies.”

9. On 20th June, 1934, Mr. Groves asked the Minister of Health how many cases of diphtheria and deaths from that disease have occurred in Dewsbury in immunised children since immunisation was first started in that town; and how many months had elapsed since the last inoculation before diphtheria developed in these cases?

Sir H. Young : The following is the information furnished by the local authority on this subject.

The number of cases of diphtheria and deaths therefrom occurring in “immunised” children was as follows :—

		1932		1933		1934 (1st January to 13th June)
Cases	...	13	...	26	...	23
Deaths	...	4	...	2	...	3

The following table, summarised from Sir Hilton Young's figures, shows the number of cases which occurred within six months of the last injection and those which occurred between the seventh and twenty-first month respectively, the latter being indisputably cases of diphtheria in fully immunised children.

Months since last injection	1932		1933		1934
1st to 6th	13	...	6	...	2
7th to 21st	nil	...	20	...	21

It will be noted that allowing for the six months interval since the last injection (which is claimed as the period necessary for immunity to develop) this table alone reveals 41 cases of diphtheria occurring in fully "immunised" children.

10. Dr. E. Ashworth Underwood, Deputy M.O.H. for Leeds, wrote in regard to the immunisation of children in that city that :

"it was found that the ordinary prophylactics such as T.A.M. (toxoid-antitoxin mixture) gave results which were quite unsatisfactory." (*Medical Officer*, 26th May, 1934.)

In the light of the foregoing evidence it is manifestly absurd for statements to be made implying that the protection afforded by inoculation is complete, such as the following typical one by the M.O.H. for Beckenham :—

"Diphtheria can be regarded as an 'optional disease,' as far as the individual is concerned." (*Annual Report for 1928*.)

IMMUNISATION HAS NO EFFECT ON SEVERITY OF ATTACK.

It is frequently asserted that diphtheria is less fatal in the inoculated. In the *Brit. Med. Jour. (Epit. of Current Med. Lit., p. 92)* a statement of M. Fayot's is quoted (*Thèse de Paris, 1933, No. 487*) that it has been observed in France that : "Diphtheria following inoculation does not present any special features. It may be severe and even fatal . . ."

FALLACY UNDERLYING FAVOURABLE REPORTS.

In addition to the foregoing positive evidence of the failure of inoculation to immunise, there remain to be considered the fallacies which afford an explanation of apparently favourable statistics. These are dealt with in Section 9 (see pp. 52-54 post).

One of the chief fallacies giving rise to erroneous conclusions was indicated by Dr. Friedberger in the course of his address to the Berlin Medical Society in 1931, in the course of which he maintained that :—

"As regards active immunization against diphtheria . . . its introduction had not caused any change in the occurrence of epidemics, and that all the statistics as to its success, which mainly emanated from American sources, were based on the erroneous conclusion that the decline in the incidence of diphtheria was due to immunization, whereas the immunization was being carried out when the disease was already showing a tendency to abate." (*The Lancet*, March 14th, 1931, p. 598.)

SECTION 6.

THE DANGERS OF "SCHICK" IMMUNISATION

A SERIES OF DISASTERS

A SERIES OF DISASTERS 1919-1933

The following is a list of such "Schick" inoculation disasters as have been officially reported; they undoubtedly represent but a small proportion of the accidents that have occurred all over the world in connection with the practice.

1. In 1919, at Dallas, Texas, U.S.A., ten children were killed and sixty others made seriously ill by toxin-antitoxin which had passed the tests of the New York State Health Department.

The Mulford Company, at Philadelphia, the manufacturers, paid damages in every case.

2. In 1924, twenty-five children in Bridgewater and twenty in Concord, U.S.A., were poisoned by toxin-antitoxin. Many had high fevers, and their arms turned black and swelled to two or three times their normal size.

3. In 1924 (September) of 40 children immunised with toxin-antitoxin in a Home for infants at Baden, near Vienna, six died and a number suffered from skin necroses of various sizes at the site of the injection.

The mixture had been tested on guinea-pigs and declared non-toxic. As the result of an investigation Prof. von Pirquet advised the Austrian Ministry of Health to stop the inoculations, and since that time the practice has been forbidden in Austria.

4. In 1928, *The Lancet* of February 4th (p. 249), refers to "a more recent Russian disaster" (*Bull. Hygiene*, August, 1927, p. 667) in which "14 children received toxin in place of anatoxin (i.e., toxoid); eight of them died within two weeks, four of polyneuritis within a month and two recovered after symptoms of general intoxication."

5. In 1927 also there were five deaths in immunised children in China, thirty-seven others being made seriously ill.

6. In 1928, at Bundaberg, Australia, twelve children out of seventeen who were inoculated with toxin-antitoxin died, the five others being critically ill for some time. The material had been issued and declared safe by the Public Health Department of Queensland.

The Government Medical Officer, after making post-mortem enquiry, stated as the only explanation "that latent properties in the serum suddenly became active and turned it into a virulent poison." Several families were wiped out, and "the tiny victims spent a night of intense suffering."

7. In 1930, at Medellin, Columbia, South America, forty-eight children were inoculated, with the result that many were taken ill during the same night, one died the following afternoon, fourteen others within sixty hours and two more within six weeks—a total of sixteen deaths.

According to the report in *The Lancet*, (October 24th, 1931, p. 923), this disaster was due to toxin being given at the third injection instead of toxoid. The symptoms recorded were: "extreme restlessness, convulsions, fever, diarrhoea, vomiting, and severe pain at the site of the injection." Almost the whole of the 48 children were ill for three or four weeks, "fever and convulsions being common."

8. In 1932, at Charolles in France, 172 children were immunised with anatoxin (toxoid). All were taken ill soon afterwards, developing local abscesses with abundant suppuration, necessitating surgical intervention in several cases. In one case the child died. The parents of the children demanded an official enquiry, but no explanation of the tragedy has so far been forthcoming.

It is significant that only a month before this disaster the Paris Med. (November 12th, 1932) declared of anatoxin (toxoid) "that it is devoid of toxicity."

9. In 1933 (April) a number of children in Italy were immunised with a single injection of anatoxin.

In the province of Chiavari over 30 inoculated children were gravely affected, some being paralysed in arms and legs, others having their sight injured. One child died. In Venice and Rovigo severe symptoms, including paralysis, supervened and death occurred in ten cases.

The Italian Government ordered the entire stoppage of diphtheria immunisation; and the National Serotherapeutic Institute at Naples, which supplied and tested the material, was, according to Press reports, closed, and the director and his assistant arrested.

Since in many of the above disasters, after investigation, it was alleged that some mistake had been made either in manufacture or administration, they have been described separately.

At the same time, it must be pointed out that the explanations offered cannot be regarded as satisfactory, since it is difficult to understand why, if no fault lay with the immunising mixtures in themselves, it has been thought necessary to replace them by different preparations.

ALL THE DANGERS THAT NOW FOLLOW ARE INHERENT EFFECTS OF THE MIXTURES THEMSELVES, AND CANNOT BE ASCRIBED EITHER TO "TECHNICAL ACCIDENT" OR "HUMAN ERROR."

SECTION 7.

THE INHERENT DANGERS
OF "SCHICK" IMMUNISATION

THE INHERENT DANGERS OF "SCHICK" IMMUNISATION

Each immunising material has in turn been declared to be harmless, while each subsequent one has been recommended on the ground that its reactions may be expected to be less severe than those of its predecessor.

In the circulars issued by Public Health authorities all over the country, it is continually stated that the injection of the mixture has been, and will be, attended by no ill effects.

The Chief Medical Officer of the Board of Education, Sir George Newman, has described the procedure as a "safe, practical and efficient method of protection." (*The Journal of Clinical Research*, April, 1934, p. 64.)

No reference to the disasters which have been recorded in various parts of the world, nor to the severe reactions which are a frequent sequel to the inoculation, is made in these official statements, and even in the *Memorandum* (Med. 170), issued by the Ministry of Health for the guidance of Medical Officers of Health, only the barest mention of possible local reaction to toxoid is to be found.

With regard to the usual claim that the treatment is "painless and harmless," no more definite refutation could be imagined than that contained in the statement, recently made by Prof. A. V. Hill, F.R.S., in the course of a defence of vivisection, that:—

"babies suffer when vaccinated, **children when immunized against diphtheria**, soldiers when inoculated against typhoid, etc." (*The Leader*, May 15th, 1934, p. 2.)

Each of the chief immunising substances will now be discussed in turn:—IT IS TO BE PARTICULARLY NOTED THAT THE REACTIONS DESCRIBED ARE DIRECTLY DUE TO THE PECULIAR NATURE OF THE MATERIAL USED, AND ARE ADMITTEDLY NOT TO BE ATTRIBUTED TO ANY ERROR IN MANUFACTURE OR ADMINISTRATION.

TOXIN-ANTITOXIN

1. The most serious danger is the occurrence of ANAPHYLAXIS and the ARTHUS PHENOMENON (Mass Gangrene).

Since this is shared by another preparation, TOXOID-ANTI-TOXIN, it is separately dealt with on pp. 44 to 49. An account will also be found in the *Medical World*, April 6th, 1934 (p. 151).

2. Dr. C. D. Mercer, of West Union, Iowa, investigated the dangers of toxin-antitoxin and reported on them in the *Annals of Internal Medicine* (January, 1929, p. 668). He found that in

125 persons between the ages of six and twenty years immunised with three injections of T.A.T. supplied by the State Board of Health, the percentage of albuminuria was increased from the normal of 10 per cent. to 20 per cent. He concluded :—

“Toxin-antitoxin is not a harmless preparation and should not be given children in a haphazard way.”

3. The *British Medical Journal*, March 23rd, 1929 (Epit. of Current Med. Lit., p. 51) quotes a report from a Health Clinic in the city of Atlanta, U.S.A., which states that :—

“In the past three years the horse-serum product had given rise to severe reactions in at least 40 per cent. (of cases).”

4. An annotation in the *Lancet*, January 30th, 1932, contains a report of the investigations of two research workers (A. T. Glenny and M. Barr) :—

“It seems evident from these experiments that a toxin-antitoxin mixture which proved harmless when tested on guinea-pigs might be poisonous in a child, and it is not easy to devise any simple method of testing which would expose dangerous mixtures with certainty. . . . It is clear that toxin-antitoxin mixtures should be given up.” (p. 252.)

As far back as 1922, Sir Frederick Andrewes, addressing the Society of Medical Officers of Health (February 17th) warned them that :—

“The injection of toxin-antitoxin might be dangerous unless it were prepared by persons of the highest skill. Fatal cases had occurred abroad. There were only a few really competent for this work, and if the procedure were carried out on a large scale, a scheme of State control would be necessary.”

5. Yet we find that, according to *The Medical Officer*, July 6th, 1929 :—

“In New York the mixture is used more often than toxoid.”

6. A. G. Ogilvie, M.B., M.R.C.P., Med. Registrar, Royal Victoria Infirmary, Newcastle-on-Tyne, confesses in the *Medical World*, December 5th, 1930 :—

“It is as well to mention here that reactions, sometimes severe, have occurred after T.A.T. injections. . . .” (p. 351.)

7. In the *Journal of the Medical Society of New Jersey*, January, 1930, it is stated that :—

“The widespread use of toxin-antitoxin is too well known to necessitate elaboration. During the period covered by the increased use of toxin-antitoxin and therapeutic serums, the incidence of serum disease has also increased. . . . A 1927 report showed . . . that 28.2 per cent. of 1,199 patients who received diphtheria antitoxin subsequently developed serum disease.”

TOXOID-ANTITOXIN

1. Dr. Saunders, M.O.H. for Cork, stated in an article on the subject of reactions in the *Lancet*, April 15th, 1933, that:—

"It must not be forgotten that reactions of the utmost severity may occasionally be encountered with toxoid-antitoxin, and many cases come under our notice in which the whole of the upper arm has been involved in an intense inflammatory reaction accompanied by marked prostration." (p. 795.)

2. Dr. Geo. Chesney, Assistant Medical Officer of Health for Poole, reported in the *British Medical Journal*, July 15th, 1933, a case of "acute scarletiform dermatitis following injection of toxoid-antitoxin" in a girl of 16. Two days after the second injection the skin rash "flared up in an acute dermatitis, spreading from the neck and chest to the back, the abdomen, then to the arms, legs and head, until the whole body was involved, with the exception of the hands and feet." This condition lasted between two and three weeks before showing signs of improvement (p. 98).

3. The *Lancet*, February 4th, 1928 (p. 249), reported that:—
"Almost all the immunization in this country is carried out with toxoid-antitoxin mixture."

4. In "*Recent Advances in Vaccine and Serum Therapy*," by Alex. Fleming, F.R.C.S., and G. F. Petrie, M.D. (Churchill, 1934), it is stated that:—

"The most extensively used diphtheria prophylactic in England since 1924 has been a toxoid-antitoxin mixture." (p. 428.)

5. In answer to a question in the House of Commons on March 15th, 1934, "whether toxoid-antitoxin is still used for diphtheria immunisation in this country; and whether there has been any alteration in the strength of the mixtures used during the last twelve months?" the Minister of Health replied:—"The answer to the first part of the question is in the affirmative; and to the second in the negative."*

6. That there is dissatisfaction with toxoid-antitoxin is revealed by the statement of Dr. E. Ashworth Underwood, Deputy M.O.H. for Leeds, namely, that on account of the "quite unsatisfactory" results of the ordinary prophylactics such as T.A.M., he had used formol toxoids of high values—between two and six times the strength of those employed in America. (*Medical Officer*, May 26th, 1934.)

*See also the Minister of Health's answer to a further question by Mr. Tom Groves, on April 23rd, 1934, quoted on p. 49 post.

The last part of this statement should be compared with that of Dr. E. A. Underwood which follows.

TOXOID; FORMOL-TOXOID; RAMON'S TOXOID; ANATOXINE

1. Parke Davis and Co., in *Therapeutic Notes*, November, 1929, No.5, state that :—

"Toxoid-antitoxin . . . is said to be free from the danger of the rather severe reactions which are occasionally produced by diphtheria toxoid alone." (See also "*Recent Advances in Vaccine and Serum Therapy*," Fleming and Petrie, 1934, p. 429.)

2. In *The Medical Officer*, July 6th, 1929, it is stated :—

"We know that undiluted diphtheria toxoid was used in London five years ago and the reactions in a small group of adults were so severe that its use was for a time abandoned."

"Park used toxoid in 1923 and has used it a good deal since. He has published some results showing a larger percentage of local and general reactions in patients receiving toxoid than in those receiving mixture (toxin-antitoxin)."

"Out of 144 patients in the series reported by G. F. and G. H. Dick who had been immunized with Ramon's toxoid (anatoxine) 44 did not complete their treatment. The suggestion is that many of them failed to do so because of reactions, and the authors are so impressed by this aspect of the matter that they give details of nine severe reactions in this group."

3. In an article in the *Lancet*, July 23rd, 1932, by R. A. O'Brien and H. J. Parish, of the Wellcome Physiological Research Laboratories, it is stated that :—

"The only obstacle in the way of the universal use of toxoid is the tendency to cause local and general reactions in older children." (p. 176.)

4. According to the *Lancet*, March 17th, 1934 :—

"The wider use of toxoid has been delayed here, just because of its tendency to produce more severe reactions than our public health authorities are accustomed to. . . ." (p. 582.)

5. In *Clinical Excerpts*, Vol. 8, No. 11, November, 1933, it is stated :—

"The disadvantage of the toxoid is that it may produce unpleasant, though not dangerous, reactions in older children and adults."

6. In an *Editorial* on "The Prevention of Diphtheria" in the *Lancet*, May 14th, 1932 (p. 1052), it is stated :—

"It has been objected, however, that toxoid at full strength, especially in adults, gives rise to troublesome reactions." (p. 1053.)

According to this article, Surgeon Capt. Dudley, Medical Officer at Greenwich Hospital School, finds that not only are the reactions following Ramon's toxoid more frequent age for age than after toxoid-antitoxin floccules, but that they are more severe. He considers "that in adults and protein-sensitive reactors, in whom toxoid may produce very unpleasant symptoms, floccules should always be used." (p. 1053.)

7. In the *Memorandum* (Med. 170) issued by the Ministry of Health in November, 1932, it is admitted that a strong reaction to formol toxoid may be expected IN 5 PER CENT. OF CHILDREN OF ALL AGES.

8. In "*Recent Advances in Vaccine and Serum Therapy*" (1934, p. 430), Alex. Fleming, F.R.C.S., and G. F. Petrie, M.D., write :—

"It is recorded that in some children inoculations of toxoid have been followed by a flare up of tuberculous foci (Aubertin and Boudou, 1932)."

9. In *The Journal of Clinical Research* (Vol. XX, No. 2, April, 1934, p. 65), the statement is made :—

"It (toxoid antitoxin) does not cause the unpleasant reactions seen in the administration of toxoid."

"Anatoxine . . . is apt to cause unpleasant reactions."

10. Dr. E. Ashworth Underwood, Deputy M.O.H. for Leeds, writing of the immunisation of about 1,000 children with formol toxoid of high value, confessed :—

"A difficulty which is associated with the use of these powerful materials is that a certain proportion of children—roughly eight per cent.—are liable to show rather severe reactions after injection with the prophylactic." (*Medical Officer*, May 26th, 1934.)

ALUM TOXOID

1. Introduced on account of the failure of toxoid-antitoxin (see page 28), its "reactions" are described in an article by the Medical Officer of Health for Cork, Dr. Saunders, as varying from slight to severe and as including abscess formation. (*Lancet*, April 15th, 1933.)

He wrote :—

"Generally speaking, the severe reactions to alum-toxoid have been more limited in extent (to those of toxoid-antitoxin described on p. 38), but have had sharply demarcated edges and have been of a more livid type." (p. 795.)

2. The *Lancet*, November 12th, 1932, contains an article dealing with alum toxoid, which has been used extensively by Park and Shroder in New York, and by Wells, Graham, and Havens in Alabama. It is there stated :—

" There seems to be a distinct tendency for the material to produce rather obstinate indurations, and occasionally even cold abscesses." (p. 1069.)

3. According to the *Lancet*, March 17th, 1934 (p. 582), Park found that the reactions though " not in the least harmful . . . are annoying."

Referring to Dr. Saunders' reports, it stated :—

" It was clear that the reactions he encountered were more numerous and more severe than would have followed the use of toxoid-antitoxin mixtures, toxoid-antitoxin floccules, and probably toxoid by itself."

" Baker and Gill found that local and general reactions were not any more severe with alum-toxoid than when ordinary toxoid was used. In this country such a statement might be taken as the faint praise that damns."

" In the Alabama series it is mentioned that some children showed local and even severe general reactions, and that eight developed abscesses which required incision. . . ."

4. In "*Recent Advances in Vaccine and Serum Therapy*" (Fleming and Petrie, 1934), it is stated :—

" The addition of alum to toxoid increases its efficiency as an antigen, but it increases the reaction, and so it has attained no popularity for human immunization." (p. 430.)

DIPHTHERIA TOXOID (ALUM-PRECIPITATED)

The very latest prophylactic to be issued is derived from Diphtheria Toxoid by precipitation with aluminium potassium sulphate. According to the makers (Mulford) it is not to be confused with Alum Toxoid. It has been exclusively used, they state, in Chicago since the autumn of 1932. After noting the " variability of commercial toxoid brands in general," they claim a further advantage of this preparation over others in that it is free from albumen, so that " severe reactions and the production of the anaphylactic state are avoided. In these days of serum treatment for a variety of diseases, with compulsory immunization before journeys to other countries, this is of no small importance."

This is at least a confession of the dangerous nature of other prophylactics, and our suspicions of similar disadvantages in the newer preparation are by no means allayed when we read in the firm's special *circular* that:—

"Reactions are not greater than would be expected from ordinary Toxoid."

"The resulting 'lump' may not disappear for four to five weeks." (Brochure issued by Sharp and Dohme, Ltd., Mulford Biological Laboratories, May, 1934.)

We are well acquainted with the reactions to be expected from toxoid and previously described.* The small experience with this substance in regard both to time and distribution precludes the possibility of any evidence of value as to its effects at present. We must wait until time reveals them, as it has done in the case of each of its predecessors.

For descriptive details of the various "immunizing" preparations dealt with in this chapter, the reader should refer to "*Recent Advances in Vaccine and Serum Therapy*," by Alex. Fleming, F.R.C.S., and G. F. Petrie, M.D. (published by Churchill, 1934).

*See page 39.

SECTION 8.

DANGERS INHERENT IN ALL MIXTURES
CONTAINING ANTITOXIN

THE ARTHUS PHENOMENON

ANAPHYLAXIS
MASS GANGRENE

DANGERS COMMON TO BOTH TOXIN-ANTITOXIN AND TOXOID-ANTITOXIN

The danger of producing ANAPHYLAXIS ("Arthus phenomenon") is common to all mixtures which contain ANTI-TOXIN, for this is derived from an animal serum.

It is important to note that in answer to a question in the House of Commons on March 15th, 1934, Sir Hilton Young admitted that toxoid-antitoxin is still used in this country, and that there has been no alteration in the strength of the mixture during the past twelve months. (see p. 38, par. 5.)

1. In *Therapeutic Notes* (November, 1929, No. 5) issued by Parke, Davis and Co., it is stated:—

"It is obvious that a preparation containing horse-serum introduces the possibility of sensitizing the recipient to a subsequent dose of horse-serum, as the great majority of antitoxins employed therapeutically are developed in this animal."

2. Writing in the *Journal of the American Medical Association*, January 9th, 1926, Dr. Chester Stewart, Assistant Professor of Pediatrics in the University of Minnesota Medical School, warns his readers that:—

"As a result of the wide-spread employment of toxin-antitoxin preparations for active immunization of children against diphtheria, clinicians undoubtedly will encounter an increased frequency of the incidence of anaphylactic reaction following subsequent administration of serums to these sensitized patients." (p. 113.)

One of his cases, who had been immunised a year previously, was injected with antitetanic serum and at once developed alarming reactions: very rapid breathing and diffuse redness of the skin which, a week later, broke out into enormous weals all over the body, with severe swelling of the tongue, face, hands and feet; this was followed at intervals of a few days by four similar attacks.

In six other cases the symptoms, writes the author, "were of such severity as to be alarming"; in one case the temperature rose to 104° F., and the child had severe vomiting attacks every half-hour for twelve hours.

THE ARTHUS PHENOMENON

Stedman's Medical Dictionary, 1923, defines it as:—

"A phenomenon of anaphylaxis in which a rabbit, after receiving several injections of normal horse serum, develops an abscess, edema, or gangrene at the site of the last injection, becomes cachectic, and dies."

It was first described by Maurice Arthus, a French bacteriologist, in 1903. Lucas and Gay called attention to similar effects in children in 1909. Dr. Harrison Tumpeer, in an article in the *American Journal of Diseases of Children*, February, 1933 (pp. 343-354), declared that:—

“Undoubtedly subsequent reactions in the nature of the Arthus phenomenon occurred following additional use of horse-serum for other reasons, but were disregarded or not sufficiently appreciated until 1927.”

He went on to add:—

“With the advent of the antitoxin era, a new situation developed in which sensitisation to horse-serum was produced by three injections at weekly intervals of the minute quantities of horse-serum present in the ordinary toxin-antitoxin mixtures. . . .”

1. In 1927 Gatewood and Baldridge described six cases, the severest of which occurred in a nurse of twenty-five. The particulars they gave in the *Journal of the American Medical Association*, April 2nd, 1927 (p. 1068), are briefly as follows:—

The nurse was Schick-negative in January, 1925, but, “in spite of this she was given toxin-antitoxin mixture in three doses, February 6th, 13th and 20th.” She developed diphtheria in November, 1925, and was given antitoxic serum in one arm and the corresponding hip. This was followed by acute general enlargement of the superficial lymph nodes. On the ninth day a further injection of serum in the other arm and corresponding thigh resulted in the arm becoming red, swollen and tender, and by the second day both arm and leg were twice the normal size. By the ninth day after the second injection the skin of the thigh lesion had become a black eschar; free incision yielded no pus although the tissue was necrotic. On the twenty-sixth day the discharge from the wound became purulent. On incision, “the abscess cavity was found to extend from the knee to the hip and around the thigh to the inner aspect. In the previous wound there presented a mass of necrotic tissue which was removed. It involved subcutaneous fat, fascia lata and muscle, and was a mass the size of a fist.” The left arm, which had undergone all the changes of the thigh, was later incised, yielding a thick yellow necrotic material. The nurse eventually recovered.

The authors predicted that the Arthus phenomenon might logically be expected to be reported more frequently with the increased use of horse-serum.

2. In 1931, Dr. I. Harrison Tumpeer described the following case (*Journal of American Medical Association*, April 25th, 1931, pp. 1373-6):—

A girl of five years had received the usual three injections of toxin-antitoxin in 1926 when one year old. In 1927 she was pronounced Schick negative. She developed diphtheria in 1930, and an injection of serum was given in the left gluteal region, followed three days later by a second dose on the opposite side.

In three hours the buttock began to swell and became extremely tender, until eventually the whole region became black and gangrenous. By the ninth day a deep area of ulceration appeared at the margin separating the necrotic tissue from the normal.

On the twelfth day the child began to complain of *extreme* pain over the right lower quadrant of this area, and an incision yielded thick yellow pus. From now onwards the condition spread over the abdominal wall and thigh until the sixteenth day, when a large necrotic mass 6" by 8" was cut away under anaesthesia. The author writes: "This large piece of gangrenous skin with subcutaneous fat and fascia was lifted off much as a lid from a stove . . . the underlying muscles lay exposed almost entirely independent of fascia which sloughed, and a large amount of which had come away in the discharge. After apposition, the muscles lay exposed much as in an anatomic dissection." In spite of assiduous irrigation of the wound she became rapidly worse, *suffering considerable pain*. Following a blood transfusion on the twenty-seventh day of illness, she became cyanotic, vomited, lost consciousness, and died a few hours afterwards.

3. The third case was reported by Dr. H. E. Irish and Dr. E. C. Reynolds in 1933, and occurred in a boy aged two years and four months. (*Journal of American Medical Association*, February 18th, 1933, p. 490.) He developed symptoms suggesting meningitis and was given three injections of anti-meningococcic serum on three successive days, and a further dose four days later. The three usual toxin-antitoxin inoculations had been performed at the age of eleven months. The serum was injected into the buttocks and was followed by an urticarial eruption over the entire body, the edematous swelling of the face being sufficient to close the eyes. Delirium with a temperature of 103°F. persisted for three days, when he became rigid. He was then given a further injection of serum in the left buttock; within an hour the site became purple, and on the following day a similar injection into the right buttock resulted in a similar reaction. During the next few days the areas of purple swelling extended from the buttocks over the front of the abdomen and right thigh, and large blebs about one and a half inches in diameter appeared; six days later these gave rise to a bloody watery discharge.

At this time the child was admitted into hospital, and presented gangrenous areas on both buttocks, both sides of the abdomen, and the thighs. There was a patch of pneumonia in the right lung and a left otitis media. Despite the removal of large masses of necrotic tissues, surgical drainage and three blood transfusions, the child died in twenty-one days from admission to hospital.

It is necessary to emphasise once more that this phenomenon of mass gangrene is one which may occur without previous warn-

ing in any child who has been at any time subjected to any so-called immunising inoculations containing antitoxin, should a further injection of horse-serum be given. It is not a particularly comforting thought for any parent to feel that the possibility of such a tragedy hangs over his child for an indefinite period, no matter how carefully the injection has been carried out, and despite all precautions in manufacture. **The danger is inherent in serum-therapy.**

Dr. Harrison Tumpeer remarks:—

"It is reasonable to suppose that many individuals inoculated with toxin-antitoxin derived from horse-serum might subsequently require horse-serum for such conditions as scarlet fever, pneumonia, tetanus, hæmorrhage, or even diphtheria itself. In such individuals there would be present to some degree at least, the laboratory conditions of Arthus." (*Jour. of Amer. Med. Assoc.*, April 25th, 1931, p. 1373.)

Longcope and Rakemann have stated that "the injection of horse-serum in small or large amounts in human beings is always followed sooner or later by the development of (specific) hypersensitiveness of the skin. . . ." (*Jour. of Exper. Med.*, 27:341; 1918.)

Nor is the problem affected by the smallness of the dose; for in an article on this very point in *The Journal of Immunology* (Vol. IX, No. 1, January, 1924, p. 7), Dr. S. B. Hooker of Boston writes:—

"That such a tiny amount of horse-serum (about 0.01 mil. in the total individual dose of toxin-antitoxin, and 0.005 mil. in the test dose) should suffice to develop allergic conditions in previously non-sensitive human beings was regarded as a phenomenon of considerable biological interest."

Gatewood and Baldrige (*Jour. of Amer. Med. Assoc.*, April 2nd, 1927, p. 1071), after referring to the definite demonstration by Hooker of the production of skin hypersensitiveness in otherwise normal and insensitive individuals by the injection of toxin-antitoxin, go on to declare that:—

"The statement from most commercial biological laboratories as well as many workers in the field of immunity, that the amount of horse-serum in toxin-antitoxin mixtures is too small to be sensitizing, seems to us to be untenable."

This conclusion is borne out by a recent fatal case (see p. 16 ante), and by Dr. Harrison Tumpeer's experience that:—

"Minute quantities of foreign protein are highly antigenic. Clinically this fact has become amply demonstrated in some of the severe reactions to scarlet fever antitoxin which resulted in the accusation of extreme toxicity against that agent. The accusers had overlooked the fact that most of the children receiving scarlet fever antitoxin had previously received horse-serum in the form of toxin-antitoxin." (*Jour. of Amer. Med. Assoc.*, April 25th, 1931, p. 1375.)

FREQUENCY OF REACTIONS

The probable frequency of such occurrences to be expected in actual practice is indicated by Gatewood and Baldrige in a table which they give showing the percentage of reactions after giving diphtheria antitoxin in a series of cases. (*Jour. of Amer. Med. Assoc.*, April 2nd, 1927, p. 1071.) The figures are as follows:—

	No. of Cases	Immediate local reaction	Delayed local reaction	General reaction	Total reactions
Toxin-antitoxin. No other serum ...	87	27	17	1	50.5%
T.A.T. Also therapeutic dose of serum ...	26	20	2	0	84.6%
Former therapeutic dose of serum. No toxin-antitoxin ...	19	9	3	0	63.1%
Neither T.A.T. nor other serum given previously ...	158	19	1	0	12.6%

In the *Journal of Immunology* (Vol. IX, No. 1, January, 1924, p. 17), further tables are given showing that over 70 per cent. of children (116) who had been immunised by toxin-antitoxin (three injections) were hypersensitive to horse-serum, compared with 50 per cent. of those children who had no previous injections (90). In adults the percentage of hypersensitiveness was 90 in the immunised, compared with 74 in those who had not received any injection of serum or toxin-antitoxin.

The whole difficulty is increased by the fact that there is no certain method of deciding beforehand if any given case is likely to react unfavourably; for, as Dr. Harrison Tumpeer states: "Reactions may occur even when skin tests are negative." (*Jour. of Amer. Med. Assoc.*, April 2nd, 1927, p. 1376.)

Although the foregoing reactions were in connection with TOXIN-ANTITOXIN, the danger of their occurrence is equally great in the case of TOXOID-ANTITOXIN, a preparation declared by the Minister of Health to be in use in this country,* since the substance which causes them, the ANTITOXIN, IS PRESENT IN BOTH.

Dr. J. Chamberlain in his prize essay read to the Guy's Hospital Physical Society, on "*The Nature and Clinical Significance of Anaphylaxis*," in 1931, declared:—

"The increasing frequency with which human interference permits injections of antigenic substances into the circulating blood, betokens an increasing number of fatal anaphylactic reactions and other less significant forms of sensitization." (*Medical World*, Jan. 1931, p. 476.)

*See Hansard, March 15th, 1934; quoted on page 38 (par. 5).

A copy of the "*Medical World*," April 6th, 1934, containing an account of the dangers of Anaphylaxis,† with illustrations of the cases of mass gangrene already described, having been sent to each Member of Parliament, the Minister of Health was asked by Mr. Groves on April 23rd, 1934 :—

"Whether his attention had been called to cases that have occurred of anaphylaxis due to the injection of toxin-antitoxin; and whether, in view of the use in this country of toxoid antitoxin for diphtheria immunization, he will take steps to safeguard the public against possible similar results of such injections?"

The Minister of Health, Sir Hilton Young, replied :—

"The answer to the first part of the question is in the affirmative. With regard to the second part, anaphylaxis is not a phenomenon peculiar to diphtheria immunization. I am advised that the relevant facts are widely recognised, and I do not consider it necessary to take any special action in the matter."

As we go to Press two further cases of anaphylactic mass-gangrene have come to our notice. One, the less severe, since the patient recovered, was that of a nurse who had been "immunized" and found Schick negative; three years later she developed diphtheria, was admitted to Hospital, and given an injection of antitoxic serum. The severe reactions so closely resembled those described in the case on page 45 that the details may be omitted; they are fully reported by John A. Maroney, M.D., in *The New England Journal of Medicine*, July 19th, 1934 (p. 106).

The second case, which ended fatally, is fully described in a Report by Frederick E. Ross, M.D., in the *Journal of the American Medical Association*, Vol. 103, No. 8 (August 26th, 1934, p. 563). He writes :—

"A boy, aged 4 years, had been given toxin-antitoxin for diphtheria immunization a year previously. November 22nd (1933?), he sustained a scalp injury and the attending physician administered a prophylactic injection of tetanus antitoxin. Three days later he had a temperature of 104°F., a generalized erythematous rash, vomiting and a sore throat with cervical adenitis. The symptoms so closely resembled those of scarlet fever that the physician administered a therapeutic injection of scarlet fever streptococcus antitoxin in the buttock. The efflorescence cleared up in a few hours, but the site of the injection immediately became indurated and erythematous, and a lesion developed which spread with such fulminating intensity that when seen, December 1st, the skin and subcutaneous tissues of the entire thigh, hip and abdomen were involved in a large necrotic sloughing mass. The patient died as the result of sepsis that evening."

† "*Some Little Understood Effects of Serum Therapy*," by M. Beddow Bayly, M.R.C.S., L.R.C.P.

SECTION 9.

STATISTICAL FALLACIES

STATISTICAL FALLACIES

1. ALTERATIONS IN DIAGNOSIS

In this country, at least, all statistics purporting to show the beneficial effect of immunisation on the incidence of diphtheria must be viewed with grave suspicion owing to a practice of juggling with the diagnosis which now exists.

Just as in the case of smallpox it has become customary to refuse to diagnose the disease in a child who has been vaccinated within the previous ten years (in order to prove the efficacy of vaccination), so now, according to the admission of the Medical Officer of Health for Ipswich (see *East Anglian Times*, February 22nd, 1934) it is the practice NOT TO CLASSIFY AS CASES OF DIPHTHERIA persons who, after immunisation, develop sore throats even though the presence of the Klebs-Loeffler bacillus (hitherto considered diagnostic of the disease) can be demonstrated in them.

MILD CASES IN "IMMUNISED" CANNOT BE DIPHTHERIA

This entire change of front regarding the diagnosis of diphtheria once more completely invalidates future statistics for scientific purposes. It will be remembered that the original change of diagnosis from the clinical one to the bacteriological, when antitoxic serum was introduced in 1894, was the means whereby thousands of mild sore throats were included under the heading of diphtheria, and thus led to an apparent fall in the case-fatality rate. (See p. 11, par. 2.)

In the present instance the refusal to classify cases as diphtheria on the ground of the mildness of the symptoms is not only statistically dishonest, but scientifically unjustifiable, inasmuch as the fact is ignored that mild cases of diphtheria have always existed.

Clinical Excerpts of January, 1934, contains an account of the disease as it occurred in the middle of the 18th century, taken from John Fothergill's "*Account of the Sore Throat attended with Ulcers.*" From this it appears that "in Kidderminster, of 242 cases treated with 'bark and opium' only seven died, and of these six had neglected early treatment" (a case-fatality of only 2.8 per cent.)

In a paper read before a branch of the British Medical Association, and reported in the *Brit. Med. Jour.*, December 7th, 1861, Dr. William Carr said:—

"From my personal observations of this disease there are two forms of diphtheria: (1) the malignant and acute; (2) the simple. The former has a high rate of mortality, higher than that of any other disease with which I am acquainted; the latter, on the contrary, seldom proves fatal." (p. 606.)

TYPICAL CLINICAL CASES NOT DIPHTHERIA IN "IMMUNISED"
UNLESS KLEBS-LOEFFLER BACILLUS PRESENT.

A further complication in diagnosis has been introduced by the MEDICAL RESEARCH COUNCIL, who state in their *Special Report*, No. 115 (1927), that before any diagnosis of diphtheria can be made in a Schick negative reactor, even though he presents all the clinical features of the disease,

"Diphtheria bacilli must be obtained in culture from the individual's throat or nose, and proved virulent by guinea-pig test." (p. 17.)

As we have seen previously, the K.L.B. (diphtheria germ) may be absent in as many as 40 per cent. of cases of clinical diphtheria (see p. 6); so that using one or other of these methods of "exclusion" it would be quite possible to rule out a very large proportion of cases occurring in Schick "immunised" or negative persons from the classification of diphtheria.

2. ERRORS OF CLASSIFICATION.

The second source of error lies in the omission to present comparable classes of children when comparing the incidence among inoculated with that among uninoculated.

When the differences in the social status, hygienic surroundings, nutrition and general state of health are considered, the possibilities of error due to these factors being ignored are seen to be enormous.

Age classification is another factor which it can be demonstrated has led to serious errors.

Dr. J. F. C. Haslam points out:—

"The incidence and mortality rates of diphtheria vary from age to age."

And referring to American statistics he says:—

"There is nothing in the data cited in support of this or of most other immunisation campaigns to show that the groups compared were of similar susceptibility or were exposed to equal risk." (*Recent Advances in Preventive Medicine* [Churchill, 1930], p. 296.)

In Dr. Graham Forbes' *Report* (No. 115) issued by the Medical Research Council (1927), it will be found that 76 per cent. of the CHILDREN IMMUNISED (in Edinburgh) were between 5 and 10 years of age, only 21.2 per cent. being under this age. (p. 61.)

But of the total number of deaths from diphtheria by far the larger portion occur in children under five years of age:—

In Edinburgh, 1925, 76 per cent. under five, 24 per cent. between 5 and 15. (p. 61 of *Report*.)

In Liverpool, 1916-1925, of 1,366 deaths, 65 per cent. were in children under age of 5 years. (p. 42 of *Report*.)

In Liverpool, 1925, 69 per cent. of deaths were under 5, and 24 per cent. between 5 and 10 years.

It is obvious that when, in seeking to prove the efficacy of immunisation, these two classes are lumped together and the total deaths among "immunised" and "non-immunised" given, the greater number of deaths are bound to be among the NON-IMMUNISED.

IN JUDGING EVIDENCE AS TO DIMINISHED DEATH-RATES AMONG "SCHICK" IMMUNISED NO STATISTICS SHOULD BE ACCEPTED WHICH OMIT PARTICULARS AS TO AGE-GROUPING, BY WHICH SOME COMPARISON BETWEEN INOCULATED AND NON-INOCULATED CLASSES CAN BE SCIENTIFICALLY EFFECTED.*

3. ERRORS DUE TO NATURAL VARIATIONS IN INCIDENCE.

In estimating any effect upon the incidence of diphtheria of any preventive measure it is necessary to take into account the curve of incidence over a large number of years, both before and after its introduction, owing to the normal wide fluctuations of the disease apart from any form of treatment. This has already been stressed in the quotations from Dr. Friedberger, the eminent German authority. (See pp. 10 and 30, ante.)

Prof. Ulrich Friedemann, of Berlin, has also pointed out that:—

"Diphtheria has a typical time curve . . . with a constant ebb and flow. It appears as an epidemic extending over some 30 years, disappears, and then begins another period of 30 years." (*The Lancet*, Aug. 4th, 1928, p. 213).

The following letter from Dr. Stephen Rowland, M.O.H. for Northampton, which appeared in *The Lancet*, December 24th, 1927, should be borne in mind in this connection. He wrote:—

"The mere fact of there being a lull in the number of notifications of diphtheria following immunization does not necessarily prove anything. During the summer I received a visit from a Swedish M.O.H., when, amongst other matters, we discussed diphtheria. He told me that it had almost disappeared from his town of late years, and on my asking if it was due to toxin-antitoxin immunization, my friend replied: 'Certainly not. Whatever be the cause, it is not immunization, for I have not practised it and do not intend to do so, as I do not believe in it.' Up to the time of writing we have had a very considerable fall in the number of notifications of diphtheria in Northampton, and for some months it has apparently been almost absent from the town, there not having been a single case in a child of or under school age. Again, this happy state has not been brought about by toxin-antitoxin immunization, for it has never been attempted here." (p. 1366.)

*Even when the statistics show the age-grouping of the diphtheria cases, it must be remembered that the uninoculated class differs in other respects from the inoculated (stamina, general health, social conditions, etc.).

SECTION 10.

THE FALLACY OF THE THEORY OF
IMMUNITY

THE TRUE CAUSE OF DIPHTHERIA

THE PREVENTION OF DIPHTHERIA

THE FALLACY OF THE THEORY OF IMMUNITY

The theory of immunity is based on the assumption that even a mild attack of the disease, produced by the inoculation of the toxin, will provoke a condition of "immunity" in the body which will protect it from further attack. It is believed that both in the naturally acquired and the artificially induced disease protection is brought about by the development of "antitoxin" in the blood of the individual.

The following facts are difficult to reconcile with this theory :—

1. *Quain's Dictionary of Medicine* (1902) states :—

"One attack of diphtheria confers no prolonged immunity upon its subject. Even during convalescence the patient has been known to develop the disease afresh, and this may be repeated more than once."

2. Dr. Claude Buchanan Ker (Medical Superintendent, City Hospital, Edinburgh), in "*A Manual of Fevers*" (1912) wrote :—

"Second attacks are quite common, many persons suffering twice, or even more frequently, from diphtheria." (p. 240.)

3. Goodall and Washbourne, in "*A Manual of Infectious Disease*" (1896), state :—

"It is uncertain how far one attack of this disease protects against a second. Certainly relapses and second attacks are not very rare. Some authors, indeed, consider that one attack predisposes to another. This is doubtful; but probably one attack confers little, if any, protection." (p. 116.)

4. L. A. Garcia (*Arch. Latino-Amer. de Pediatria*, January, 1929), remarks that :—

"All physicians have seen cases of repeated diphtheria, and it is difficult to believe that the immunity which spontaneous diphtheria cannot give to the child may be produced by vaccination."

5. Dr. C. W. Hutt, M.O.H. for Holborn, reported in *The Lancet*, November 7th, 1925, the case of a boy who, two years after the three routine injections, developed diphtheria for the third time in his life. (p. 964.)

6. The following comment is made in the *Bulletin of Hygiene* for June, 1934, under the heading "Vital Statistics and Epidemiology" :—

"[Diphtheria].—Repeated attacks are not unusual. Zischinsky has seen several examples of three or four attacks in the same child and one case in a child who had six attacks in 18 months. The second attack in several cases ended fatally."

7. Professor Jürgens, discussing the value of immunisation before the Berlin Medical Society (*The Lancet*, March 14th, 1931), remarked that :—

"[Diphtheria] antitoxin had never been found in the blood of diphtheria convalescents or in cases of diphtheria after death. There was, therefore, in his opinion, no certain proof of the value of immunization against diphtheria." (p. 598.)

8. In addition to these difficulties there are certain startling admissions made by the Medical Research Council in its publication on Diphtheria (1923-24) concerning the nature of the TOXIN on which the whole immunising process is founded. They state :—

"We are completely in the dark regarding its chemical composition and the mechanism of its elaboration."

Then, owing to the fact that the toxin has to be grown on beef broth, they complain of the resulting preparation :—

"We are never dealing twice with the same mixtures."

Finally, after detailing other difficulties, they conclude :—

"All these factors make toxin manufacture a very complicated matter."

9. Professor W. W. C. Topley, in "*An Outline of Immunity*" (1933), states that as regards active immunisation :—

"The only way of dealing with this question in such a book is by a frank admission of our inability to answer it satisfactorily."

10. Dr. J. E. R. McDonagh, in his *Nature of Disease Journal* (Vol. I, 1932, p. 69), maintains :—

"The whole subject of immunity is built upon an entirely false basis, and in many instances it would be better to treat the symptoms and let the cycle run its normal course than to prevent infection with a so-called "immuno-agent," which at the very best can produce no more than temporary immunity."

He points out (p. 192) that :—

"Every infection carries with it the weapons which are ultimately to destroy it"; and warns us that their action "may be seriously interfered with by the production of man-made milder infections."

THE CAUSE OF DIPHTHERIA

ANCIENT BELIEF

The belief that a close relationship exists between epidemic diseases and bad sanitation and lack of hygiene generally was taught by Hippocrates, the father of medicine, and held the field for two thousand years.

Known as the "miasmatic" theory, it was not until the advent of the erroneous Pasteurian doctrines towards the end of the last century that it became temporarily obscured.

Sydenham, the "English Hippocrates" elaborated it in the 17th century, and even as late as 1894 it was maintained by Dr. Charles Creighton in his classical "*History of Epidemics in Great Britain*."

FAILURE OF MODERN THEORIES

Though disregarded, this theory has never been superseded, and in spite of 50 years' research by believers in the Pasteurian "germ" origin of disease, none of the modern theories, as Dr. C. A. Gill admits in his work, "*The Genesis of Epidemics and the Natural History of Disease*," can claim to provide an adequate explanation of the cause of epidemics.

As a leading article in the *Times* of August 13th, 1930, pointed out:—

"The nature of these and other variations has exercised the minds of physicians and bacteriologists during many years, but it cannot be said that any very clear views about them have been formulated."

CORROBORATION OF ANCIENT BELIEF.

In a paper he read before a branch of the British Medical Association at Maidstone on October 25th, 1861, Dr. William Carr declared:—

"All my carefully conducted inquiries induce me to believe that the disease comes from drain-poison. All the cases into which I could fully inquire have brought conviction to my mind that there is a direct law of sequence in some peculiar conditions of atmosphere between diphtheria and bad drainage." (*Brit. Med. Jour.*, Dec. 7th, 1861, p. 607.)

In the discussion which followed, Dr. Monceton enlarged upon this conception, stating his impression that infection

"arose from what might be called an error in nature's destructive assimilation of refuse matter. Effete animal and vegetable organisms were intended to decay back to the inorganic world as harmlessly as they emanated from it; but by thermal, electric, or some other perturbation, leaves, vegetables, animal matter, and sewage might at any time be evolving in the process of decay abnormal and damaging products, and this over an infinitely extended area." (*Ibid.*)

Béchamp's teaching regarding the function of microzymas, together with modern knowledge regarding the chemistry of colloids, supply the connecting links between the extraordinarily accurate conclusions based upon long and painstaking observation (which we see were held by medical scientists before the misleading teachings of Pasteur and his satellites of the laboratory cast their paralysing spell over medical thought) and a complete technical understanding of the problem which the intellect demands.

But a detailed discussion of this subject lies outside the scope of this pamphlet. The student will have no difficulty in pursuing it upon the basis of these brief hints.

The connection between diphtheria and sewage was again emphasised in 1894 in Quain's *Dictionary of Medicine* as follows:—

"There is no doubt that exposure to sewage emanation is a fruitful source of diphtheria . . . the statistics of the association between the two are very positive."

Parkes and Kenwood, in the 1907 edition of "Hygiene and Public Health," say:—

"Faulty sanitary surroundings (drainage and health nuisances) tend to the production of diphtheria in the same way, namely, by endangering a morbid condition of the tonsils favourable to the growth of the diphtheria contagion if implanted thereon."

This clearly indicates that an antecedent morbid change in the "soil" is necessary before any so-called diphtheria germ can grow therein; thus establishing that the latter is not the true cause of the disease. (See pp. 6 and 7 ante.)

RECENT CONFIRMATION

Dr. Austin Priestman, M.O.H. for Folkestone, writing in the *Medical World*, February 6th, 1931, reported that investigation "shows in interesting and conclusive fashion the definite effect of school buildings, their construction and sanitation, on the spread of diphtheria. The highest incidence was observed in those schools where sanitation is most deficient and ventilation and lighting the least satisfactory. The brightest and airiest school showed the lowest incidence, and the incidence throughout all the schools placed them in exact order of sanitary virtue."

"Moreover, the incidence indicated the schools where malnutrition in the children is most conspicuous." (p. 627.)

According to T. J. Nicholl, F.R.C.S.I., Assistant M.O.H. for Dover:—

"The causes which predispose a person to infection are:—

- (a) Damp atmosphere, which lowers the vitality of the upper respiratory tract.
- (b) An unhealthy condition of the tonsils and mucous membrane of the naso-pharynx is a very suitable soil on which the bacillus may thrive.
- (c) The debilitating effects of other infectious disease, such as measles, scarlet fever, whooping cough, and mumps." (*The Journal of Clinical Research*, April, 1934, p. 60.)

THE PREVENTION OF DIPHTHERIA

When once the principles involved in the causation of diphtheria are grasped, it will be realised how futile, unscientific and anti-social are all attempts at artificial immunisation.

The main preventive measures which alone can be successful in eliminating diphtheria epidemics "embrace wholesome food, hygienic clothing, a sufficiency of fresh air and an adequate elimination of waste-products," to quote the words of J. E. R. McDonagh which refer to infections in general. (*Nature of Disease Journal*, Vol. 2, 1933, p. 193.)

It is obvious that the necessary reforms, educational, social, sanitary, to bring out this desirable state of things will be indefinitely delayed and thwarted if the current orthodox belief is allowed to gain ground that the unpleasant results of their neglect, namely, epidemic diseases, can be more easily and cheaply avoided by inoculating helpless children.

This is the main reason why this type of "preventive medicine" is so strenuously supported by vested interest, for not only are vast fortunes derived from the manufacture of the various immunising materials, but, what is even more important, all those powerful interests which are directly or indirectly adversely affected by the march of social progress stand to gain by the promulgation and adoption of this vast delusion which is being thrust upon the public.

Indifferent alike to individual lives of children or to national health, this modern Juggernaut of Vested Interest crushes onward, until, faced with an enlightened public opinion, the deadliest foe of tyranny, it shall be overthrown.

We may fitly conclude this survey of the important problem of artificial immunisation against diphtheria in the words of James Gordon Cumming, M.D., D.P.H.; in an article in the *Journal of the American Medical Association*, March 4th, 1922, he wrote :—

"The eradication of diphtheria will not come through the serum treatment of patients, by the immunization of the well, or through the accurate clinical and laboratory diagnosis of the case and the carrier followed by quarantine; rather it will be attained through the mass sanitary protection of the populace subconsciously practised by the people at all times." (p. 632.)

We shall find no more practical advice than that given by Dr. Austin Priestman, Medical Officer of Health for Folkestone, when, in an article on "*Epidemic Diphtheria*" in the *Medical World*, February 6th, 1931, he declared :—

"Rather than attempt wholesale immunization by artificial means we should adopt the same plan of campaign against bacillus diphtheriæ as we adopted against the bacillus of tuberculosis—namely, provide better ventilated, better lighted and better equipped schools, and feed all children who need feeding." (p. 627.)

SECTION II.

SUFFERING CAUSED TO ANIMALS
IN THE MANUFACTURE AND
TESTING OF SERA

SUFFERING TO ANIMALS INVOLVED

The cruelty to animals involved in the preparation of anti-toxin and immunising mixtures falls under four heads:—

- (1) As regards the horses (or other animals) used in the manufacture of serum.
- (2) As regards the guinea-pigs used for standardising the toxin.
- (3) As regards the guinea-pigs used for standardising the serum obtained from the horse (or other animal).
- (4) As regards testing for organism in throat swabs.

1. For the production of serum horses are injected with gradually increasing doses of toxin, or toxoid, two or three times a week. The following description is quoted from Hewlett and McIntosh's "*A Manual of Bacteriology*" (Churchill, 1932):—

"Individual horses vary in their susceptibility to the toxin, so that care has to be exercised with the earlier injections. The injections are given subcutaneously over the shoulder, and produce local swelling with some rise of temperature and general disturbance, lasting two or three days. When this has passed away the inoculation is repeated, a larger dose being administered provided the reaction due to the former was not too severe." (p. 294.)

"A horse to be of value should after three months' treatment yield an antitoxic serum containing not less than 300 units per cubic centimetre. The required potency having been ascertained, as shown by the test described below, the horse is bled with aseptic precautions, the blood is allowed to coagulate, and the serum is separated and filled into sterile bottles." (p. 295.)

"Wadsworth (1927) gives the detailed record of a horse which in 9 years gave 161 bleedings of about 8 litres." ("*A System of Bacteriology*," 1929, p. 356.)

In some cases the blood corpuscles are reinjected into the horse,

"which is thereby deprived only of plasma and is consequently able to withstand more frequent and larger bleedings." ("*A Manual of Bacteriology*", p. 295.)

In the Medical Research Council's *Report on diphtheria* (1923) it is stated:—

"Among the ill-effects that may follow toxin injections, the most severe are paralysis, and death of the horse with fatty degeneration of the heart and degenerative changes in the kidney. A chronic malady sometimes supervenes in animals which have undergone for some years continuous courses of anti-toxin-production. . . . The animal soon becomes ill and eventually dies with amyloid degeneration of the spleen and liver, and with hepatic and peritoneal hæmorrhages." "Even with the greatest precautions a certain proportion of animals fall victims to acute toxæmia." (pp. 131 and 134.)

In "*Recent Advances in Vaccine and Serum Therapy*" (1934), we learn that some reactions in the horse are an advantage to the manufacturer, however painful to the animal, for

"Ramon noted an increase in the amount of antitoxin in the blood of horses when sterile abscesses happened to form at the site of the inoculation, and from this observation he was led to produce artificial sterile abscesses by mixing the toxin with a tapioca preparation." (p. 2.)

2. In Hewlett's "*A Manual of Bacteriology*" (1932) it is stated in regard to standardisation of toxin (p. 297) that

(a) The minimum lethal dose of a toxin is estimated by finding the amount which injected into a series of guinea-pigs kills on the fourth or fifth day. (Those that die after this period do not count.)

(b) The least amount of toxin which, mixed with a unit amount of antitoxin (standard) just kills a guinea-pig on the fourth or fifth day is known as the L+ dose, and is the amount of the test toxin now usually employed for standardising each fresh batch of antitoxin. (See 3 (b) post).

In "*A System of Bacteriology*" (Medical Research Council, 1929, Vol. V, p. 90), we may read:—

"By the end of 24 hours after inoculation the animal usually manifests symptoms of acute illness. It will be found cowering in a corner of its cage, with coat ruffled and with definite dyspnoea. It is cold to the touch . . . the weight diminishes rapidly up to the moment of death in about 4 days. A dose of diphtheria culture or toxin which will kill in this time is spoken of as the 'minimum lethal dose' (M.L.D.). Multiples of this quantity will kill guinea-pigs in as short a time as 24 hours with symptoms correspondingly violent and acute."

"When the culture is not in its most virulent state or the dose is small, the animal may survive for a week, or even much longer, and finally succumb in a state of marasmus. The local lesion, at first soft, becomes indurated; necrosis sets in and the whole affected area may slough and leave a slowly healing granulating wound."

The pathological condition produced by the injection into the guinea-pig is described in Hewlett's "*A Manual of Bacteriology*" (1932) as follows:—

"At the site of the inoculation hæmorrhagic oedema forms, hæmorrhages occur in the serous membranes, and especially in the adrenals, while the renal epithelium and the liver cells undergo cloudy degeneration." (p. 290.)

3. In the same text-book (p. 299) it is stated:—

"The unit of diphtheria antitoxin may for practical purposes be defined as an amount which neutralises approximately 100 M.L.D.s of diphtheria toxin for the guinea-pig."

Note : Standardisation of antitoxin serum is effected by two methods :—direct and indirect.

(a) In the first, the amount of serum which, when mixed with the M.L.D. of toxin and injected into a guinea-pig, is sufficient to prevent death, is ascertained. The number of units contained is then calculated.

(b) In the second, the amount of serum which, when mixed with the L + dose of toxin (previously described), protects a standard guinea-pig, is used as the basis of calculation.

The reason for the adoption of the second method is the unreliability of the first, but the underlying technicalities are far too complicated for explanation here.

In either method the antitoxin serum is injected in graduated dilutions into a whole series of guinea-pigs and those in whom the antitoxin is not sufficient to neutralise the toxin succumb in varying periods as previously described.

4. In addition to the suffering involved in the above procedures, further inoculations into animals are frequently performed in the course of tests of the virulence of organisms found to be present in the throats of patients. After the specimen from a throat-swab has been incubated on a special medium, in a test-tube,

"The whole of a young serum slope* is emulsified in saline and injected subcutaneously into a 250 grm. guinea-pig. If the strain be virulent, death will usually ensue in one or two days with the characteristic post-mortem appearances." (*"A Manual of Bacteriology,"* Hewlett and McIntosh, 1932, p. 311.)

The sufferings which precede death, and the post-mortem changes to be observed, have been described under heading 2 on the previous page.

In the Ministry of Health's *Report on Diphtheria*, No. 10 (p. 30), a different method is described in which the culture to be tested is injected "intra-cutaneously," i.e., into the abdominal skin of a guinea-pig which has previously been depilated "preferably by pulling the hair out."

This, they inform us, can be done "with probably less pain than is associated with the prolonged irritation which, at times, follows the application of depilatory barium sulphide paste." Additional guinea-pigs, previously injected intracardially (in the heart) with antitoxin, are used as controls; these latter animals are employed over and over again.

*The culture grown upon the sloping surface of the culture-medium in a test-tube.